-77-

Claims

1. A compound of formula I:

$$X \xrightarrow{A} Y$$
 $X \xrightarrow{X} NR_1R_2$
 I

5 wherein

15

A is selected from O and S;

X is selected from

phenyl optionally substituted with up to 5 substituents each independently selected from halo, C₁-C₄ alkyl and C₁-C₄ alkoxy;

thienyl optionally substituted with up to 3 substituents each independently selected from halo and C_1 - C_4 alkyl; and

C₂-C₈ alkyl, C₂-C₈ alkenyl, C₃-C₈ cycloalkyl and C₄-C₈ cycloalkylalkyl, each of which may be optionally substituted with up to 3 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)n- where n is 0, 1 or 2, -CF₃, -CN and -CONH₂;

Y is selected from dihydrobenzothienyl, benzothiazolyl, benzoisothiazolyl, quinolyl, isoquinolyl, naphthyridyl, and thienopyridyl, each of which may be optionally substituted with up to 4 or, where possible, up to 5 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, nitro, acetyl, - CF₃, -SCF₃ and cyano;

Z is selected from H, OR₃ or F, wherein R₃ is selected from H, C₁-C₆ alkyl and phenyl C₁-C₆ alkyl;

R₁ and R₂ are each independently H or C₁-C₄ alkyl;

or pharmaceutically acceptable salt thereof.

5

10

20

- 2. A compound as claimed in claim 1, wherein A is O.
- 3. A compound as claimed in claim 1, wherein A is S.
- 4. A compound as claimed in any one of the preceding claims, wherein one of R_1 and R_2 is H.
- 5. A compounds as claimed in any one of the preceding claims, wherein one of R_1 and R_2 is H and the other is methyl.
- 6. A compound as claimed in any one of the preceding claims, wherein the compound possesses the stereochemistry defined in formula Π

$$X \xrightarrow{A} Y$$
 $X \xrightarrow{X} NR_1R_2$
 $X \xrightarrow{Z} II$

7. A compound as claimed in claim 6, wherein the compound possesses the stereochemistry defined in formula III

$$X \xrightarrow{A Y} NR_1R_2$$
III

- 8. A compound as claimed in any one of the preceding claims wherein Z is H.
- 9. A compound as claimed in any one of the preceding claims, wherein

5

10

X is unsubstituted phenyl or phenyl which is mono-, di- or tri-substituted with substituents independently selected from halo, C₁-C₄ alkyl and C₁-C₄ alkoxy.

- 10. A compound as claimed in claim 9, wherein X is unsubstituted phenyl or phenyl which is mono-substituted with fluorine.
 - 11. A compound as claimed in any one of the preceding claims, wherein Y is dihydrobenzothienyl optionally substituted with up to 5 substituents each independently selected from halo, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, C_1 - C_4 alkyl- $S(O)_n$ where n is 0, 1 or 2, nitro, acetyl, -CF₃, -SCF₃ and cyano.
 - 12. A compound as claimed in claim 11, wherein Y is unsubstituted dihydrobenzothienyl or dihydrobenzothienyl which is mono-substituted with fluorine.
- 13. A compound as claimed in any one of the claims 1-10, wherein Y is benzothiazolyl or benzoisothiazolyl, each of which may be optionally substituted with up to 4 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, nitro, acetyl, -CF₃, -SCF₃ and cyano.
- 14. A compound as claimed in claim 13, wherein Y is unsubstituted benzothiazolyl, unsubstituted benzoisothiazolyl, benzothiazolyl which is mono-substituted with CH₃ or benzoisothiazolyl which is mono-substituted with CH₃.
- 15. A compound as claimed in any one of the claims 1-10, wherein Y is thienopyridyl optionally substituted with up to 4 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, nitro, acetyl, -CF₃, -SCF₃ and cyano.
- 16. A compound as claimed in any one of claims 11-15, wherein the point of attachment of the group Y to the O or S atom is attachment at the 7 position.

WO 2004/043931 PCT/US2003/031512

- 17. A compound as claimed in any one of claims 11-15, wherein the point of attachment of the group Y to the O or S atom is attachment at the 4 position.
- 18. A compound as claimed in any one of the claims 1-10, wherein Y is quinolyl, isoquinolyl or naphthyridyl, each of which may be optionally substituted with up to 5 substituents each independently selected from halo, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, C_1 - C_4 alkyl- $S(O)_n$ where n is 0, 1 or 2, nitro, acetyl, -CF₃, -SCF₃ and cyano.

5

20

- 19. A compound as claimed in claim 18, wherein the point of attachment of the group Y to the O or S atom is attachment at the 4 position.
 - 20. A compound as claimed in claim 18, wherein the point of attachment of the group Y to the O or S atom is attachment at the 5 position.
- 15 21. A compound as claimed in claim 18, wherein the point of attachment of the group Y to the O or S atom is attachment at the 6 position.
 - 22. A pharmaceutical composition comprising a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-21, together with a pharmaceutically acceptable diluent or carrier.
 - 23. A compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-21, for use as a pharmaceutical.
- 24. A compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-21, for use as a selective inhibitor of the reuptake of both serotonin and norepinephrine.
- 25. A compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-21, for use in the treatment of a disorder associated with serotonin and norepinephrine dysfunction in mammals.

WO 2004/043931 PCT/US2003/031512

26. A compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-21, for use in the treatment of a disorder selected from selected from depression, OCD, anxiety, memory loss, urinary incontinence, conduct disorders, ADHD, obesity, alcoholism, smoking cessation, hot flushes/flashes and pain.

5

- 27. The use of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-21, for the manufacture of a medicament for selectively inhibiting the reuptake of serotonin and norepinephrine.
- 28. The use of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-21, for the manufacture of a medicament for the treatment of a disorder associated with serotonin and norepinephrine dysfunction in mammals.
- 15 29. The use as claimed in claim 28, wherein the disorder is selected from depression, OCD, anxiety, memory loss, urinary incontinence, conduct disorders, ADHD, obesity, alcoholism, smoking cessation, hot flushes/flashes and pain.
- 30. The use as claimed in claim 29, wherein the disorder is selected from depression, urinary incontinence and pain.
 - 31. The use as claimed in any one of claims 28-30, wherein the disorder is pain.
- 32. A method for selectively inhibiting the reuptake of serotonin and norepinephrine in mammals, comprising administering to a patient in need thereof an effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-21.
- 33. A method for treating disorders associated with serotonin and norepinephrine dysfunction in mammals, comprising administering to a patient in need thereof an effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-21.

WO 2004/043931 PCT/US2003/031512

-82-

34. A method as claimed in claim 33, wherein the disorder is selected from depression, OCD, anxiety, memory loss, urinary incontinence, conduct disorders, ADHD, obesity, alcoholism, smoking cessation, hot flushes/flashes and pain.

5

35. A method as claimed in claim 33 or 34, wherein the disorder is pain.